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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,196	01/24/2002	Y. Tom Tang	039386-0220	3875

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/744,196	TANG ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on February 6, 2007 has been entered. Claims 3-11 remain pending and under examination.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 3-11 under 35 U.S.C. 101 for not being supported by either a specific, substantial and credible asserted utility, or a well-established utility, is maintained for reasons of record. Applicant's arguments filed February 6, 2007 have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

- Applicant argues that the specification asserts a specific and substantial utility for a polynucleotide encoding a MACP-2 protein. The MACP-2 protein is associated with cell proliferation. This assertion is supported by the specification and the claims as originally filed. Specifically, Applicant points to the specification at page 14, lines 14-16 as evidence that the polynucleotides are asserted to be useful in the diagnosis, treatment or

prevention of cell proliferative and immune disorders. Applicant asserts that proliferative disorders include cancer, such as cancer of the brain, breast, cervix, gastrointestinal tract, ovary, lung, prostate and uterus (page 25, lines 2-6). Given this disclosure, Applicant argues that the assertion of utility is specific and substantial.

- In response to Applicant's argument, a substantial utility is one that defines a "real world" use, which does not require carrying out further search to identify or reasonably confirm a "real world" context of use. In this case, Applicant has listed several disorders that MACP-2 could diagnose, treat or prevent. MACP-2 has not been demonstrated as a diagnostic marker for any of these proliferative disorders, and thus the utility is not substantial.

- Applicant argues that the utility is credible in view of Table 1 of the specification, showing that the clone of MACP-2 was isolated from a cDNA library derived from a prostate cancer tumor (Table 4, page 53). Applicant argues that MACP-2 was found to be expressed in libraries from diseased breast, lung, prostate and brain. Applicant argues that the nucleotide sequence encoding MACP-2 was found in 71.4% of cDNA libraries that were proliferative in nature (Table 3). Applicant concludes that MACP-2 is associated with cell proliferative disease.

  - In response to this argument, the presence of MACP-2 in proliferative-type libraries is not evidence that MACP-2 is a diagnostic marker. Many proteins are expressed in tumors, not just diagnostic marker proteins. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use.

In this case, MACP-2 would have to be accepted as available for use a diagnostic marker for disease. (The utility that Applicant is arguing is the diagnostic use of MACP-2). Based on the presence of MACP-2 in various cancer cDNA libraries, one of ordinary skill in the art would not consider MACP-2 available for use a diagnostic marker for disease without further characterization and research into the expression and association of MACP-2 with specific types of cancer.

- Applicant argues that the utility is credible in view of MACP-2's homology to a 190 kDa precursor to the protein tenascin (Table 2, page 51). Tenascin is involved with cell proliferation (page 1, line 32 through page 2, line 8). Vollmer *et al.* (*Biochem. Cell. Biol.*, 1994, 72:505-514) reports the expression of tenascin in carcinogenesis, particularly, with tumors of the endometrium, breast and prostate (page 505). Applicant also points out that tenascin functions in glioma and neural development, and cell attachment through an RGD-dependent receptor (Bourdon and Ruouslahti, *J. Cell. Biol.* 1989, 108:1149-1155). Applicant argues that the utility is well known because of the well established utility of tenascin, the sequence similarity with MACP-2, and the similar expression profile of MACP-2. Applicant points to Example 10 of the USPTO Revised Interim Utility Guidelines Training Materials. Applicant argues that Example 10 is similar to the instant situation, where sequence homology to a ligase, claimed as a ligase, is deemed supported by a well established utility as a ligase.
    - In response to Applicant's arguments, the level of sequence identity to tenascin is not sufficient to demonstrate utility for MACP-2. Applicant's analysis of tenascin hinges on Example 10 of the Utility Guidelines. The Office has reviewed

Example 10 for its relevance to the instant situation. Example 10 offers the scenario that where a high level of homology to a known protein (such as a ligase) is observed, and the similarity between the novel sequence and the consensus sequence of known proteins (ligases) is high (95%), and the next highest level of homology to the novel sequence is only 50% and encodes a different protein (not a ligase), there is a well established utility for the novel protein. This scenario does not fit the instant situation. In the instant case, the novel sequence does not encode a known protein. MACP-2 is not a well known protein that has consensus sequences, as compared with known proteins such as ligases. When examining the levels of homology of Applicant's SEQ ID NO: 2 to other sequences, Applicant has not provided evidence of a common encoded protein. For example, Applicant notes the homology to tenascin, which is associated with glioma and neural development, and is expressed in various cancers (though not confirmed as a cancer diagnostic marker). It has not been demonstrated that other sequences having similar levels of homology to SEQ ID NO: 2 also encode tenascin, or proteins with similar function. In summary, Applicant cannot rely on Example 10 of the Utility Guidelines because the scenario is different. The protein, MACP-2, is not comparable to the well known class of ligases, of Example 10.

- Applicant argues that the post-filing art confirms Applicant's asserted utility. Applicant points to MACP-2, also known as WIF-1, as associated with proliferative disease, including cancer. Steg *et al.* (*J. Molecular Diagnostics*, 2006, 8 :76-83) discloses that WIF-1 was expressed in tissue samples from 5/6 human ovarian endometrioid

adenocarcinomas, but was not expressed in normal ovarian tissue. Applicant also points to Boerboom *et al.* (*Cancer Res.*, 2006, 66:1964-1973), which discloses WIF-1 was over-expressed in ovarian granulose cell tumors and in solid pretumoral lesions in the ovaries of mice, compared with normal ovarian tissue. Applicant also points to Cebrat *et al.* (*Cancer Lett.*, 2004, 206:107-113) as evidence that WIF-1 was over expressed in intestinal adenomas compared to normal epithelial cells in APC mice, and was also over expressed in cell lines derived from murine and human mammary gland adenocarcinoma and human colon adenocarcinoma. Reguart *et al.* (*Biochem. Biophys. Res. Comm.*, 2004, 323:229-234) reports increased transcription Wnt-1 in human cell lines derived from colon and non-small-cell lung cancers, but not from mesothelioma.

- In response to Applicant's arguments, the Office has considered the references cited as evidence of utility for MACP-2. The data presented with regard to WIF-1 (Wnt-1) is useful in the process of discovering the function of MACP-2. Noting its expression is various tumors is a step in the inventive process. Applicant has identified a novel protein and characterized it based on its presence in various cell types, and its homology to other known proteins. There does not appear to be any common thread of what types of tumors MACP-2 is present or over-expressed in. MACP-2, according to the references provided, is present in a number of tumor types, at various levels. The next step in determining MACP-2 function is to see if MACP-2 can actually be used to diagnose a particular type of cancer(s). Determining the types of cancer cells that MACP-2 is expressed in is an initial step, but not conclusive of its utility as a cancer diagnostic marker.

- Applicant argues that the recent Federal Circuit case *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005) found that a specification that disclosed only ESTs failed to meet the utility requirement under 101. Fisher failed to identity a function for any EST, no EST encoded a complete gene, no EST corresponded to a protein with a known function, further research was not performed to determine if the EST was a disease marker, and further research was not performed to analyze gene expression. Applicant asserts that these failures in Fisher are not found in Applicant's disclosure.
    - In response to Applicant's argument, if one were to consider the factors that Applicant has cited from the Fisher case, Applicant's disclosure encounters some of the same failures. There is no confirmed function for MACP-2. There is no corresponding protein to MACP-2 that has the same function as MACP-2 (because no function has been confirmed). There is no further research to determine MACP-2's usefulness as a disease marker. (Although Applicant has identified the expression of MACP-2 in some cancer types, there is no evidence that MACP-2 can be used as a diagnostic marker for those cancers.) In summary, the degree of homology to tenascin is not sufficient to convey a utility to MACP-2. The post-filing literature does not convey a utility to MACP-2 because its real world use as a diagnostic marker is still being investigated and has not been confirmed. There is no common thread of a particular class of proteins to which MACP-2 shares significant homology to. The types of cancers that MACP-2 is expressed in (libraries included) are varied and the levels of expressions differ.

Further research is required to confirm the real world utility for MACP-2.

Therefore, the rejection is maintained for reasons of record.

3. Claims 3-11 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility, or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

4. Claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The polynucleotide sequences encode polypeptides that are associated with cell proliferation, a utility for which Applicant is not entitled (see rejection above). The specification does not provide adequate written description of the claimed genus.

Conclusion

5. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 4/10/07

STACY B. CHEN
PRIMARY EXAMINER